IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	N. Kasahara et al.	Art Unit :	Unknown
Serial No.:	Unassigned	Examiner :	Unknown
Filed :	January 11, 2002		

Title : GENE DELIVERY SYSTEM AND METHODS OF USE

BOX PATENT APPLICATION
Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the claims:

Cancel claims 1-40, 47, 48, 52-55, 57 and 62.

Amend claims 41, 49, 50, 51, 56 and 58-61 as follows:

--41. (Amended) A method of treating a subject having a cell proliferative disorder comprising

contacting the subject with a therapeutically effective amount of a retrovirus, comprising:

a retroviral GAG protein;

a retroviral POL protein;

a retroviral envelope;

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an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the retroviral genome, wherein a tissue-specific promoter sequence is contained within the LTR sequences at the 5′ or 3′ or 5' and 3' end of the oncoretroviral polynucleotide sequence;

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence; and

cis-acting nucleic acid sequences involved in for reverse transcription, packaging and integration in a target cell,

in a pharmaceutically acceptable carrier.

49. (Amended) The method of claim 41, wherein the oncoretroviral polynucleotide sequence is selected from the group consisting of murine leukemia virus (MLV), Moloney murine leukemia virus (MoMLV), Gibbon ape leukemia virus (GALV) and Human Foamy Virus (HFV).

50. (Amended) The method of claim 49, wherein the MLV is an amphotropic MLV.

51. (Amended) The method of claim 63, wherein the ENV protein is selected from the group consisting of murine leukemia virus (MLV) ENV protein and vesicular stomatitis virus (VSV) ENV protein.

56. (Amended) The method of claim 41, wherein the cell proliferative disorder is selected from the group consisting of lung cancer, colon-rectum cancer, breast cancer, prostate cancer, urinary tract cancer, uterine cancer lymphoma, oral cancer, pancreatic cancer, leukemia, melanoma, stomach cancer and ovarian cancer.

58. (Amended) The method of claim 41, wherein the tissue-specific promoter sequence is associated with a growth regulatory gene.

59. (Amended) The method of claim 41, wherein the tissue-specific promoter sequence is associated with probasin.

60. (Amended) The method of claim 41, wherein the heterologous polynucleotide sequence encodes a suicide gene.

61. (Amended) The method of claim 60, wherein the suicide gene is a thymidine kinase or a purine nucleoside phosphorylase (PNP).--

Add claims 63-82.

--63. The method of claim 41, wherein the retroviral envelope comprises a chimeric protein.

64. The method of claim 63, wherein the chimeric protein comprises an ENV protein and a targeting polypeptide.

65. The method of claim 64, wherein the targeting polypeptide is an antibody, a receptor, or a receptor ligand.

66. A method of treating a subject having a cell proliferative disorder comprising contacting the subject with a therapeutically effective amount of a recombinant retroviral polynucleotide, comprising:

a polynucleotide sequence encoding a GAG protein;

a polynucleotide sequence encoding a POL protein;

a polynucleotide sequence encoding a retroviral envelope;

an oncoretroviral polynucleotide sequence comprising a Long Terminal Repeat (LTR) at the 5' and 3' end of the

oncoretroviral polynucleotide sequence, wherein a target-specific promoter sequence is contained within the U3 region of the LTR sequences at the 5' or 3' or 5′ and 3′ end of the oncoretroviral polynucleotide sequence;

a heterologous polynucleotide sequence operably linked to a regulatory nucleic acid sequence; and

cis acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell.

67. The method of claim 66, wherein the polynucleotide sequence encoding a retroviral envelope encodes a chimeric protein.

68. The method of claim 67, wherein the chimeric protein comprises an ENV protein and a targeting polypeptide.

69. The method of claim 68, wherein the targeting polypeptide is an antibody, a receptor, or a receptor ligand.

70. The method of claim 66, wherein the GAG, POL and retroviral envelope polynucleotide sequences are from murine leukemia virus (MLV) or Moloney murine leukemia virus (MoMLV).

71. The method of claim 70, wherein the MoMLV is an amphotropic MoMLV.

72. The method of claim 68, wherein the ENV protein is an ecotropic protein.

73. The method of claim 68, wherein the ENV protein is selected from the group consisting of a murine leukemia virus (MoMLV) ENV protein and vesicular stomatitis virus (VSV) ENV protein.

74. The method of claim 66, wherein the heterologous polynucleotide sequence is a suicide gene.

75. The method of claim 74, wherein the suicide gene encodes a thymidine kinase or a purine nucleoside phosphorylase (PNP).

76. The method of claim 66, wherein the heterologous sequence is a marker gene.

77. The method of claim 66, wherein the regulatory nucleic acid sequence operably linked with the heterologous nucleic acid

sequence is selected from the group consisting of a promoter, an enhancer, and an internal ribosome entry site.

78. The method of claim 66, wherein the polynucleotide sequence is contained in a viral particle.

79. The method of claim 66, wherein the polynucleotide sequence is contained in a pharmaceutically acceptable carrier.

80. A method of treating a subject having a cell proliferative disorder comprising contacting the subject with a therapeutically effective amount of a recombinant replication competent murine leukemia virus (MLV), comprising:

an MLV GAG protein;

an MLV POL protein;

an MLV envelope;

an MLV polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the MLV polynucleotide sequence, wherein a target-specific promoter sequence is contained within the LTR sequences at the 5' or 3' or 5' and 3' end of the MLV polynucleotide sequence,

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence; and

cis-acting nucleic acid sequences necessary for reverse transcription, packaging and integration in a target cell.

81. A method of treating a subject having a cell proliferative disorder comprising contacting the subject with a therapeutically effective amount of a recombinant replication competent retrovirus comprising:

a retroviral GAG protein;

a retroviral POL protein;

a retroviral envelope comprising a chimeric env protein comprising a targeting ligand;

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the oncoretroviral polynucleotide sequence, wherein a tissue-specific promoter sequence is contained within the U3 region of the LTR sequences at the 5' or 3' or 5′ and 3′ end of the oncoretroviral polynucleotide sequence,

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence; and

cis-acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell.

82. A method of treating a subject having a cell proliferative disorder comprising contacting the subject with a therapeutically effective amount of a recombinant retroviral polynucleotide, comprising:

a polynucleotide sequence encoding a GAG protein;

a polynucleotide sequence encoding a POL protein;

a polynucleotide sequence encoding a retroviral envelope, wherein said envelope comprises a chimeric env protein comprising a targeting ligand;

an oncoretroviral polynucleotide sequence comprising a Long Terminal Repeat (LTR) at the 5' and 3' end of the oncoretroviral polynucleotide, wherein a tissue-specific promoter sequence is contained within the U3 region of the LTR sequences at the 5′ and/or 3′ end of the oncoretroviral polynucleotide;

a heterologous polynucleotide sequence operably linked to a regulatory nucleic acid sequence; and

cis acting polynucleotide sequences involved in reverse transcription, packaging and integration in a target cell.

REMARKS

By the present preliminary amendment, claims 1-40, 47, 48, 52-55, 57 and 62 have been cancelled. Applicants maintain the right to prosecute the canceled claims in any related application claiming the benefit of priority of the subject application. Claims 41, 49, 50, 51, 56 and 58-61 have been amended. New claims 63-82 have been added. Support for the pending claims can be found throughout the specification. No new matter as been added. Accordingly, upon entry of the preliminary amendment, claims 41-46, 49-51, 56, 58-61 and 63-82 are pending and at issue. Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be examined. Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 1/11/02

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Version with markings to show changes made

In the claims:

The claims are reiterated for the convenience of the Examiner. Claims 1-40, 47, 48, 52-55, 57 and 62 have been cancelled. Claims 41, 49, 50, 51, 56 and 58-61 have been amended as follows:

41. (Amended) A method of treating a subject having a cell proliferative disorder[,] comprising[:]

contacting the subject with a therapeutically effective amount of a retrovirus, comprising[,]:

a retroviral GAG protein;

a retroviral POL protein;

a retroviral [ENV protein] envelope;

an oncoretroviral [genome] polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the retroviral genome, wherein a [target] tissue-specific [polynucleotide] promoter sequence is contained within the LTR sequences at the 5′ or 3′ or 5' and 3' end of the oncoretroviral [genome,] polynucleotide sequence;

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence; and

cis-acting nucleic acid sequences [necessary] involved in for reverse transcription, packaging and integration in a target cell, in a pharmaceutically acceptable carrier.

42. The method of claim 41, wherein the subject is a mammal.

43. The method of claim 42, wherein the mammal is a human.

44. The method of claim 41, wherein the contacting is by in vivo administration of the retrovirus.

45. The method of claim 44, wherein the in vivo administration is by systemic, local, or topical administration.

46. The method of claim 41, wherein the contacting is by ex vivo administration of the retrovirus.

47. (Cancelled) The method of claim 41, wherein the retroviral genome is derived from a lentivirus.

48. (Cancelled) The method of claim 47, wherein the lentivirus is human immunodeficiency virus (HIV).

49. (Amended) The method of claim 41, wherein the oncoretroviral [genome] polynucleotide sequence is [derived] selected from the group consisting of murine leukemia virus (MLV), [or] Moloney murine leukemia virus (MoMLV), Gibbon ape leukemia virus (GALV) and Human Foamy Virus (HFV).

50. (Amended) The method of claim 49, wherein the [Mo]MLV is an amphotropic [Mo]MLV.

51. (Amended) The method of claim [41] 63, wherein the ENV protein [contains an ENV sequence] is selected from the group consisting of [Moloney] murine leukemia virus ([Mo]MLV) ENV protein and [Vesicular] vesicular stomatitis virus (VSV) ENV protein.

52. (Cancelled) The method of claim 41, wherein the ENV protein further comprises a target-specific ligand sequence.

53. (Cancelled) The method of claim 52, wherein the targeting specific ligand sequence is an antibody, receptor, or ligand.

54. (Cancelled) The method of claim 41, wherein the target cell is a cell having a cell proliferative disorder.

55. (Cancelled) The method of claim 41, wherein the target cell is a neoplastic cell.

56. (Amended) The method of claim [54] 41, wherein the cell proliferative disorder is selected from the group consisting of lung cancer, colon-rectum cancer, breast cancer, prostate cancer, urinary tract cancer, uterine cancer lymphoma, oral cancer, pancreatic cancer, leukemia, melanoma, stomach cancer and ovarian cancer.

57. (Cancelled) The method of claim 1, wherein the target specific polynucleotide sequence is a tissue-specific promoter sequence.

58. (Amended) The method of claim 41, wherein the tissue-specific promoter sequence is associated with a growth regulatory gene.

59. (Amended) The method of claim 41, wherein the tissue-specific promoter sequence is associated with probasin.

60. (Amended) The [retrovirus] method of claim 41, wherein the heterologous polynucleotide sequence [is] encodes a suicide gene.

61. (Amended) The [retrovirus] method of claim [41] 60, wherein the suicide gene is a thymidine kinase or a purine nucleoside phosphorylase (PNP).

The following new claims have been added:

--63. The method of claim 41, wherein the retroviral envelope comprises a chimeric protein.

64. The method of claim 63, wherein the chimeric protein comprises an ENV protein and a targeting polypeptide.

65. The method of claim 64, wherein the targeting polypeptide is an antibody, a receptor, or a receptor ligand.

66. A method of treating a subject having a cell proliferative disorder, comprising contacting the subject with a therapeutically effective amount of a recombinant retroviral polynucleotide, comprising:

a polynucleotide sequence encoding a GAG protein;

a polynucleotide sequence encoding a POL protein;

a polynucleotide sequence encoding a retroviral envelope;

an oncoretroviral polynucleotide sequence comprising a Long Terminal Repeat (LTR) at the 5' and 3' end of the oncoretroviral polynucleotide sequence, wherein a target-specific promoter sequence is contained within the U3 region of the LTR sequences at the 5' or 3' or 5′ and 3′ end of the oncoretroviral polynucleotide sequence;

a heterologous polynucleotide sequence operably linked to a regulatory nucleic acid sequence; and

cis acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell.

67. The method of claim 66, wherein the polynucleotide sequence encoding a retroviral envelope encodes a chimeric protein.

68. The method of claim 67, wherein the chimeric protein comprises an ENV protein and a targeting polypeptide.

69. The method of claim 68, wherein the targeting polypeptide is an antibody, a receptor, or a receptor ligand.

70. The method of claim 66, wherein the GAG, POL and retroviral envelope polynucleotide sequences are from murine leukemia virus (MLV) or Moloney murine leukemia virus (MoMLV).

71. The method of claim 70, wherein the MoMLV is an amphotropic MoMLV.

72. The method of claim 68, wherein the ENV protein is an ecotropic protein.

73. The method of claim 68, wherein the ENV protein is selected from the group consisting of a murine leukemia virus (MoMLV) ENV protein and vesicular stomatitis virus (VSV) ENV protein.

74. The method of claim 66, wherein the heterologous polynucleotide sequence is a suicide gene.

75. The method of claim 74, wherein the suicide gene encodes a thymidine kinase or a purine nucleoside phosphorylase (PNP).

76. The method of claim 66, wherein the heterologous sequence is a marker gene.

77. The method of claim 66, wherein the regulatory nucleic acid sequence operably linked with the heterologous nucleic acid sequence is selected from the group consisting of a promoter, an enhancer, and an internal ribosome entry site.

78. The method of claim 66, wherein the polynucleotide sequence is contained in a viral particle.

79. The method of claim 66, wherein the polynucleotide sequence is contained in a pharmaceutically acceptable carrier.

80. A method of treating a subject having a cell proliferative disorder, comprising contacting the subject with a therapeutically effective amount of a recombinant replication competent murine leukemia virus (MLV), comprising:

an MLV GAG protein;

an MLV POL protein;

an MLV envelope;

an MLV polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the MLV polynucleotide sequence, wherein a target-specific promoter

sequence is contained within the LTR sequences at the 5' or 3' or 5′ and 3′ end of the MLV polynucleotide sequence,

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence; and

cis-acting nucleic acid sequences necessary for reverse transcription, packaging and integration in a target cell.

81. A method of treating a subject having a cell proliferative disorder, comprising contacting the subject with a therapeutically effective amount of a recombinant replication competent retrovirus comprising:

a retroviral GAG protein;

a retroviral POL protein;

a retroviral envelope comprising a chimeric env protein comprising a targeting ligand;

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' end of the oncoretroviral polynucleotide sequence, wherein a tissue-specific promoter sequence is contained within the U3 region of the LTR sequences at the 5' or 3' or 5′ and 3′ end of the oncoretroviral polynucleotide sequence,

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence; and

cis-acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell.

82. A method of treating a subject having a cell proliferative disorder, comprising contacting the subject with a therapeutically effective amount of a recombinant retroviral polynucleotide, comprising:

a polynucleotide sequence encoding a GAG protein;

a polynucleotide sequence encoding a POL protein;

a polynucleotide sequence encoding a retroviral envelope, wherein said envelope comprises a chimeric env protein comprising a targeting ligand;

an oncoretroviral polynucleotide sequence comprising a Long Terminal Repeat (LTR) at the 5' and 3' end of the oncoretroviral polynucleotide, wherein a tissue-specific promoter sequence is contained within the U3 region of the LTR sequences at the 5′ and/or 3′ end of the oncoretroviral polynucleotide;

a heterologous polynucleotide sequence operably linked to a regulatory nucleic acid sequence; and

cis acting polynucleotide sequences involved in reverse transcription, packaging and integration in a target cell.

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